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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/468,145	06/06/1995	JURGEN ENGEL	Y17506/93-11	4889

909 7590 08/28/2003

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/28/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/468,145	ENGEL ET AL.	
	Examin r	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions, filed on November 12, 2002 and June 9, 2003, have been entered.

2. Applicants' amendment filed November 12, 2002 is acknowledged and has been entered. Claim 24 has been canceled. Claim 20 has been amended. Claims 20-23 are now pending in the present application.

3. Applicants' amendment filed June 9, 2003 is acknowledged and has been entered. Claim 20 has been amended. Claims 20-23 are now pending in the present application.

4. All rejections have been withdrawn in view of Applicants' amendments. However, the following new grounds of rejection have been set forth. The following Office Action is NON-FINAL.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. The amendments, filed November 12, 2002 and June 9, 2003, are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amino acid sequence of the cetrorelix with SEQ ID NO: 1.

Applicant is required to cancel the new matter in the reply to this Office Action.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification nor the claims as originally filed set forth, disclose or claim the now recited amino acid sequence of cetrorelix as now set forth in the pending specification and claims 20-23.

9. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf et al (DD 411996) and Schally et al (5198533) taken with Behre et al (1992).

The claims are directed to a method for the preparation of a sterile Cetrorelix lyophilizate, said method comprising the steps of dissolving the Cetrorelix, as forth in SEQ ID NO: 1, in aqueous acetic acid to form a solution, diluting the solution with water, adding a bulking agent (hexitol, mannitol, etc), sterile filtering, dispensing into injection vials and lyophilizing the solution, thereby obtaining a sterile Cetrorelix lyophilizate; 3% solution and pH of 2.5-3.0.

Wolf et al teach methods of preparing lyophilized synthetic LHRH, which preparation is stable at room temperature over a long period of time (page 1 of English translation; p. 3-4). Wolf et al teach the use of vehicle (i.e. mannitol; bulking agent) and buffer (i.e. acetic acid) substance for the adjustment of an optimal range of the hydrogen-ion concentration, pH (p. 2; p. 4). The prior art teaches that the application can be for veterinary medicine as an estrus-synchronization agent as well as *inter alia* in the human medicine as an agent in the case of treating fertilization disorders (p. 2-3). Wolf et al teach sterilization by filtration and that the solution is lyophilized (p. 5).

Schally et al teaches the claimed LHRH antagonist, amino acid sequence, see SEQ ID NO: 11 of the issued patent (claims). Schally et al teaches this compound in pharmaceutically acceptable acid addition salts (abstract; col. 8; cols. 15-18).

The prior art teaches the claimed invention except for the specific preparation of Cetrorelix lyophilizate.

However, Behre et al teach that GnRH antagonist Cetrorelix (an antagonistic analog of GnRH) has the potential for treatment of sex hormone-dependent diseases and male contraception (abstract). Behre et al teach the use of Cetrorelix in lyophilized for injection and was dissolved in water containing mannitol (p.

394). It is noted that Behre et al is cited to show that cetrorelix is an LHRH antagonist and that it can be prepared in the same manner as the LHRH. Behre et al uses a lyophilized cetrorelix dissolved in water and contains mannitol (p. 393; materials and methods).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a drug or compound similar to LHRH/GnRH to treat infertility in humans or veterinary medicine. The art teaches the method of preparing the LHRH, which is similar to the Cetrorelix, an antagonistic analog of LHRH/GnRH. The prior art teaches the same sequence as claimed by Applicants, see Schally et al. The Cetrorelix is a small peptide similar to LHRH and Wolf et al teaches the same method in preparing the sterile LHRH lyophilizate as claimed by Applicants, using the bulking agent (mannitol), a buffer (acetic acid) and sterile filtering, and lyophilizing the solution. The prior art (in combination) and the claimed invention prepare the cetrorelix (the same amino acid sequence, sterile and lyophilized) for the same purpose and in the same manner. The prior art of Wolfe et al and Schally et al taken with Behre et al teaches the claimed invention except for specific cetrorelix concentration of 3% and the specific pH range of 2.5 to 3.0. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine the most appropriate cetrorelix concentration to avoid clogging up the filters and the determine the correct pH range for a stable buffered solution, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). The claimed invention is prima facie obvious in view of the prior art, absent any convincing evidence to the contrary.

10. No claims are allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

N. M. Minnifield
Primary Examiner
Art Unit 1645
8/19/03

NMM